REMARKS

Claims 3, 5, 7-12, 14, 15 and 17-26 were pending and under consideration in the instant Application. With the instant amendment, claims 5, 12, 14, 15, 17 and 20-23 have been canceled, without prejudice, and claim 18 has been amended. Support for amended claim 18 can be found in the specification, at for example, page 10, lines 13-19 and claim 3 as originally filed. As the amendment of claim 18 is fully supported by the specification and claims as originally filed, it does not constitute new matter. After entry of this amendment, the pending claims are: claims 3, 7-11, 18, 19 and 24-26. A marked up version of the amended claims is attached hereto as Exhibit A. For the PTO's convenience, a clean copy of claims as pending after entry of this amendment is attached hereto as Exhibit B.

Applicants emphasize for the record that none of the amendments made herein are narrowing amendments made to overcome any "prior art" under 35 U.S.C. §§ 102 or 103. Applicants expressly reserve the right to equivalents of all claim limitations to the full extent available. Applicants expressly reserve the right to pursue any canceled subject matter in one or more related, continuation, divisional or continuation-in-part application(s).

Applicants note with appreciation that claims 3, 7-11, 19 and 24-26 have been allowed, and kindly thank the Examiner for the same. Applicants believe that amended claim 18 is likewise in condition for allowance, because it properly depends from allowed claim 3 and does not incorporate new matter. Applicants hereby request entry of the amendment into the record.

I. THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 5 and 18 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly being not enabled. Applicants respectfully submit that the cancellation of claim 5 renders the rejection of this claim moot. Applicants respectfully traverse the rejection of claim 18.

A claim is enabled if one of skill in the art, guided by Applicant's disclosure, can make and use the claimed invention without undue experimentation. *See Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916); *In re Wands*, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). The test is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is not undue. *See In re Angstadt*, 190 USPQ 214, 219 (C.C.P.A. 1976). The fact that the required experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *See In re*

Certain Limited-Charge Cell Culture Microcarriers, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom. Massachusetts Institute of Technology v. A.B. Fortia*, 227 USPQ 428 (Fed. Cir. 1985). While Applicants are required to provide an enabling disclosure, the disclosure is not required to teach, "and *preferably omits*, what is well known in the art." *See* MPEP § 2164.01 (emphasis added); *In re Buchner*, 18 U.S.P.Q.2d 1331, 1332 (Fed. Cir. 1991); *Hybritech v. Monoclonal Antibodies*, 231 USPQ 81, 94 (Fed. Cir. 1986); *Lindemann Maschinen Fabrik v. American Hoist & Derrick*, 221 USPQ 481, 489 (Fed. Cir. 1984). Among the factors to be considered when determining whether the necessary experimentation is undue are the breadth of the claims, the nature of the invention, the state of the prior art, the level of ordinary skill in the art, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *See In re Wands*, 8 U.S.P.Q.2d at 1404. In rejecting a claim for lack of enablement, the Examiner should cite any of these factors that are relevant, and specific technical reasons are *always required*. *See* M.P.E.P. at §§ 2164.01(a) 2164.04; *In re Wands*, 8 U.S.P.Q.2d at 1404.

Applicants submit that one of skill in the art, guided by the specification, would be fully enabled to practice the full scope of the method recited in amended claim 18.

Amended Claim 18 depends from allowed claim 3 and recites a method for characterizing an individual as possessing a factor contributing to an increased risk of type I diabetes or multiple sclerosis comprising, *inter alia*, determining the genotype of said individual with respect to the nucleotide present at position 883 of the TCF-1, wherein said TCF-1 gene comprises SEQ ID NO: 1, an A allele of SEQ ID NO: 1 or the complements thereof. As acknowledged by the PTO (*see* page 2, lines 6-9, of the instant Office Action), the specification enables "methods for identifying human subjects having an increased likelihood of having multiple sclerosis or type I diabetes, wherein the methods comprise detecting the presence of an A allele at position 883 of the TCF-1 gene of SEQ ID NO: 1 . . ." Accordingly, Applicants submit that amended claim 18 is enabled by the specification.

In view of the foregoing, Applicants respectfully request that the rejection of claims 5 and 18 under 35 U.S.C. § 112, first paragraph, as allegedly being not enabled, be withdrawn.

II. THE REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 12, 14, 15, 17 and 21-23 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and claim the subject matter which Applicants regard as the invention. Applicants respectfully submit that the cancellation of claims 12, 14, 15, 17 and 21-23 render the rejections of these claims moot.

In view of the foregoing, Applicants respectfully request that the rejection of claims 12, 14, 15, 17 and 21-23 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite, be withdrawn.

III. THE REJECTIONS UNDER 35 U.S.C. § 102

Claims 20 and 22 stand rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by van de Wetering *et al.*, 1992, *J. Biol. Chem.* 267:8530-8536. Applicants respectfully submit that the cancellation of claims 20 and 22 renders the rejection of these claims moot.

In view of the foregoing, Applicants respectfully request that the rejection of claims 20 and 22 under 35 U.S.C. § 102(b) be withdrawn.

IV. THE REJECTION UNDER 35 U.S.C. § 101

Claim 22 stands rejected under 35 U.S.C. § 101, as allegedly directed to non-statutory subject matter. Applicants respectfully submit that the cancellation of claim 22 renders the rejection of this claim moot.

In view of the foregoing, Applicants respectfully request that the rejection of claim 22 under 35 U.S.C. § 101 be withdrawn.

V. THE REJECTIONS OF CLAIM 20-23 UNDER 35 U.S.C. § 102

Claims 20-23 stand rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by the USB Catalog (1990). Applicants respectfully submit that the cancellation of claims 20-23 renders the rejection of these claims moot.

In view of the foregoing, Applicants respectfully request that the rejection of claims 20-23 under 35 U.S.C. § 102(b) be withdrawn.

CONCLUSION

In light of the above amendments and remarks, Applicants respectfully submit that claims 3, 7-11, 18, 19 and 24-26 satisfy all the criteria for patentability and are in condition for allowance. Applicants request that the Examiner reconsider this application with a view towards allowance and solicit an early passage of claims 3, 7-11, 18, 19 and 24-26 to issuance. The Examiner is invited to call the undersigned attorney if a telephone call could help resolve any remaining items.

No fee is believed due with this Amendment. However, pursuant to 37 CFR § 1.136(a)(3), the Commissioner is authorized to charge all required fees, fees under 37 CFR § 1.17 and all required extension of time fees, or credit any overpayment, to Pennie & Edmonds, LLP U.S. Deposit Account No. 16-1150 (order no. 1803-300-999).

Respectfully submitted,

Date: April 25, 2003

42,983
Rahul Pathak (Reg. No.)

For: Nikolaos C. George (Reg. No. 39,201)
PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, NY 10036-2711
(212) 790-9090

EXHIBIT A

MARKED UP VERSION OF AMENDED CLAIM

18. (Amended) The method of claim 3 [or 5], wherein said TCF-1 gene comprises SEQ ID NO: 1, an A allele of SEQ ID NO: 1 or the complements thereof.

EXHIBIT B

Pending Claims After Entry of Instant Amendment

3. A method for characterizing an individual as possessing a factor contributing to an increased risk of type 1 diabetes or multiple sclerosis comprising:
   (a) determining the genotype of said individual with respect to the nucleotide present at position 883 of the TCF-1 gene;
   (b) classifying said individual based on the result obtained from step (a), wherein the presence of an A allele indicates a factor contributing to an increased risk of type 1 diabetes or multiple sclerosis.

7. A method for determining the genotype of a sample comprising a nucleic acid with respect to the nucleotide present in a TCF-1 gene at position 883, comprising:
   (a) contacting the nucleic acid with an oligonucleotide probe exactly complementary to an A allele or a C allele in a region encompassing position 883 under conditions such that hybridization occurs if and only if the A allele or the C allele is present; and
   (b) detecting if hybridization occurs, wherein, hybridization to the A allele indicates that the genotype of the sample corresponds to the A allele and hybridization to the C allele indicates that the genotype of the sample corresponds to the C allele.

8. The method of Claim 7, wherein the region encompassing position 883 is amplified prior to, or concurrent with step (a).

9. A method of Claim 8, wherein said probe is selected from the group consisting of KW196 (SEQ ID NO: 8) or KW118 (SEQ ID NO: 9).

10. A method for determining the genotype of a sample comprising a nucleic acid with respect to the nucleotide present in a TCF-1 gene at position 883, comprising:
   (a) contacting the nucleic acid with one or more allele-specific primers specific for an A allele or a C allele under amplification conditions such that amplification occurs using said allele-specific primer if and only if the A allele or the C allele is present; and
   (b) detecting if amplifications occurs, wherein, amplification of the A allele indicates that the genotype of the sample corresponds to the A allele and

amplification of the C allele indicates that the genotype of the sample corresponds to the C allele.

11. A method of Claim 10, wherein said allele specific primer is GZ351B (SEQ ID NO: 4) or GZ374B (SEQ ID NO: 5).

18. (Amended) The method of claim 3, wherein said TCF-1 gene comprises SEQ ID NO: 1, an A allele of SEQ ID NO: 1 or the complements thereof.

19. A method for determining the presence of an A allele or a C allele of a TCF-1 gene in a sample comprising a nucleic acid, comprising:

(a) contacting the nucleic acid with an oligonucleotide exactly complementary to the A allele or the C at position 883 under stringent hybridization conditions; and

(b) detecting hybridization wherein, hybridization to the A allele indicates the presence of the A allele and hybridization to the C allele indicates the presence of the C allele.

24. A method for characterizing an individual as possessing a factor contributing to an increased likelihood of having an increased IgE response comprising:

(a) determining the genotype of said individual with respect to the nucleotide present at position 883 of the TCF-1 gene;

(b) classifying said individual based on the result obtained from step (a), wherein the presence of a C allele indicates a factor contributing to an increased likelihood of having an increased IgE response.

25. The method of claim 24, wherein said TCF-1 gene comprises SEQ ID NO: 1, an A allele of SEQ ID NO: 1 or the complements thereof.

26. The method of claim 24, wherein said increased IgE response is associated with atopy or allergic asthma.